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REMARKS

Claims 1, 4, 5, 7, 8-12, 14-22, 24-26, 31-36, 38 and 44 have been amended. New claims 49-54 have been added. Upon entry of this amendment, claims 1-54 will be pending. No new subject matter has been added.

Support for the claim amendments and newly added claims can be found, e.g., on pages, 5-14, and page 19, lines 20-23 of the specification, and the original claims, e.g., claims 4-5 and 38.

Applicants respectfully request that all claims be examined. Enclosed is a check for the excess claim fees. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing the attorney docket number 10274-006002.

Respectfully submitted,

Date: \_\_\_\_\_

*July 13, 2001*

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**Version with markings to show changes made**

In the claims:

Claims 1, 4, 5, 7, 8-12, 14-22, 24-26, 31-36, 38 and 44 have been amended as follows:

1. (First Time Amended) A method of preventing or treating skin conditions characterized by increased T cell activation and abnormal antigen presentation in the dermis and epidermis, comprising the step of administering to a mammal[, including a human,] an agent which binds to LFA-3 or CD2 selected from the group consisting of a CD2 polypeptide, an LFA-3 polypeptide, an anti-CD2 antibody homolog, and an anti-LFA-3 antibody homolog, in combination with a therapy selected from the group consisting of PUVA, chemotherapy and UV light. [inhibitor of the CD2/LFA-3 interaction.]

4. (First Time Amended) The method according to claim 1, wherein the [inhibitor] agent is selected from the group consisting of an anti-LFA-3 antibody homolog [homologs], and a soluble CD2 polypeptide [polypeptides].

5. (First Time Amended) The method according to claim 1, wherein the [inhibitor] agent is selected from the group consisting of anti-CD2 antibody homolog [homologs] and soluble LFA-3 polypeptide [polypeptides].

7. (First Time Amended) The method according to claim 6, wherein said soluble LFA-3 polypeptide is LFA3TIP (SEQ ID NO:8).

8. (First Time Amended) The method according to claim 4, wherein the [inhibitor] agent is an anti-LFA-3 antibody homolog.

9. (First Time Amended) The method according to claim 5, wherein the [inhibitor] agent is an anti-CD2 antibody homolog.

10. (First Time Amended) The method according to claim 8, wherein the [inhibitor] agent is a monoclonal anti-LFA-3 antibody.

11. (First Time Amended) The method according to claim 9, wherein the [inhibitor] agent is a monoclonal anti-CD2 antibody.

12. (First Time Amended) The method according to claim 10, wherein the [inhibitor] agent is a monoclonal anti-LFA-3 antibody produced by a hybridoma selected from the group of hybridomas having Accession Nos. ATCC HB 10693 (1E6), ATCC HB 10694 (HC-1B11), ATCC HB 10695 (7A6), and ATCC HB 10696 (8B8) or is monoclonal antibody TS2/9.

14. (First Time Amended) The method according to claim 8, wherein the [inhibitor] agent is a chimeric recombinant anti-LFA-3 antibody homolog.

15. (First Time Amended) The method according to claim 9, wherein the [inhibitor] agent is a chimeric recombinant anti-CD2 antibody homolog.

16. (First Time Amended) The method according to claim 8, wherein the [inhibitor] agent is a humanized recombinant anti-LFA-3 antibody homolog.

17. (First Time Amended) The method according to claim 9, wherein the [inhibitor] agent is a humanized recombinant anti-CD2 antibody homolog.

18. (First Time Amended) The method according to claim 8, wherein the [inhibitor] agent is selected from the group consisting of an Fab fragment [fragments], an Fab' fragment [fragments], an F(ab')<sub>2</sub> fragment [fragments], an F(v) fragment [fragments] and an intact immunoglobulin heavy chain [chains] of an anti-LFA-3 antibody homolog.

19. (First Time Amended) The method according to claim 9, wherein the [inhibitor] agent is selected from the group consisting of an Fab fragment [fragments], an Fab' fragment [fragments], an F(ab') 2 fragment [fragments], an F(v) fragment [fragments] and an intact immunoglobulin heavy chain [chains] of an anti-CD2 antibody homolog.

20. (First Time Amended) The method according to claim 5, wherein the [inhibitor] agent is a soluble LFA-3 polypeptide.

21. (First Time Amended) The method according to claim 4, wherein the [inhibitor] agent is a soluble CD2 polypeptide.

22. (First Time Amended) The method according to claim 20, wherein the [inhibitor] agent is a soluble LFA-3 polypeptide selected from the group [of polypeptides] consisting of AA1-AA92 of SEQ ID NO:2, AA1-AA80 of SEQ ID NO:2, AA50-AA65 of SEQ ID NO:2, and AA20-AA80 of SEQ ID NO:2.

24. (First Time Amended) The method according to claim 1, wherein the [inhibitor] agent is administered at a dose between about 0.001 and about 50 mg [inhibitor] agent per kg body weight.

25. (First Time Amended) The method according to claim 24, wherein the [inhibitor] agent is administered at a dose between about 0.01 and about 10 mg [inhibitor] agent per kg body weight.

26. (First Time Amended) The method according to claim 24, wherein the [inhibitor] agent is administered at a dose between about 0.1 and about 4 mg [inhibitor] agent per kg body weight.

31. (First Time Amended) The method according to claim 1, wherein the [inhibitor] agent is administered intravenously, intramuscularly, subcutaneously, intra-articularly, intrathecally, periostally, intratumorally, intralesionally, perilesionally by infusion, orally, topically or by inhalation.

32. (First Time Amended) The method according to claim 31, wherein the [inhibitor] agent is administered intramuscularly, intravenously or subcutaneously.

33. (First Time Amended) The method according to claim 4, wherein the [inhibitor] agent is linked to one or more members independently selected from the group consisting of anti-LFA-3 antibody homologs, soluble CD2 polypeptides, cytotoxic agents and pharmaceutical agents.

34. (First Time Amended) The method according to claim 5, wherein the [inhibitor] agent is linked to one or more members independently selected from the group consisting of anti-CD2 antibody homologs, soluble LFA-3 polypeptides, cytotoxic agents and pharmaceutical agents.

35. (First Time Amended) The method according to claim 34, wherein the [inhibitor] agent is a polypeptide consisting of a soluble LFA-3 polypeptide linked to an immunoglobulin hinge and heavy chain constant region or portions thereof.

36. (First Time Amended) The method according to claim 35, wherein said polypeptide is LFA3TIP (SEQ ID NO:8).

38. (First Time Amended) A method of preventing or treating psoriasis [skin conditions characterized by increased T cell activation and abnormal antigen presentation in the dermis and epidermis] comprising the step of administering to a mammal[, including a human,] a composition comprising an agent which binds to LFA-3 or CD2 selected from the group consisting of a CD2 polypeptide, an LFA-3 polypeptide, an anti-CD2 antibody homolog, and an

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anti-LFA-3 antibody homolog, in combination with a therapy selected from the group consisting of PUVA, chemotherapy and UV light. [chosen from the group of CD2 polypeptides, LFA-3 polypeptides, anti-CD2 antibody homologs, and anti-LFA-3 antibody homologs.]

44. (First Time Amended) The method of claim 43, wherein said soluble LFA-3 polypeptide is LFA3TIP (SEQ ID NO:8).

Pending Claims:

1. A method of preventing or treating skin conditions characterized by increased T cell activation and abnormal antigen presentation in the dermis and epidermis, comprising the step of administering to a mammal an agent which binds to LFA-3 or CD2 selected from the group consisting of a CD2 polypeptide, an LFA-3 polypeptide, an anti-CD2 antibody homolog, and an anti-LFA-3 antibody homolog, in combination with a therapy selected from the group consisting of PUVA, chemotherapy and UV light.

2. The method according to claim 1, wherein the condition is selected from the group consisting of atopic dermatitis, cutaneous T cell lymphoma such as mycosis fungoides, allergic and irritant contact dermatitis, lichen planus, alopecia areata, pyoderma gangrenosum, vitiligo, ocular cicatricial pemphigoid, and urticaria.

3. The method according to claim 1, wherein the condition is psoriasis.

4. The method according to claim 1, wherein the agent is selected from the group consisting of an anti-LFA-3 antibody homolog, and a soluble CD2 polypeptide.

5. The method according to claim 1, wherein the agent is selected from the group consisting of anti-CD2 antibody homolog and soluble LFA-3 polypeptide.

6. The method according to claim 5, wherein said soluble LFA-3 polypeptide is a soluble LFA-3 polypeptide fused to all or part of an immunoglobulin heavy chain region and all or part of a heavy chain constant region.

7. The method according to claim 6, wherein said soluble LFA-3 polypeptide is LFA3TIP (SEQ ID NO:8).

8. The method according to claim 4, wherein the agent is an anti-LFA-3 antibody homolog.

9. The method according to claim 5, wherein the agent is an anti-CD2 antibody homolog.
10. The method according to claim 8, wherein the agent is a monoclonal anti-LFA-3 antibody.
11. The method according to claim 9, wherein the agent is a monoclonal anti-CD2 antibody.
12. The method according to claim 10, wherein the agent is a monoclonal anti-LFA-3 antibody produced by a hybridoma selected from the group of hybridomas having Accession Nos. ATCC HB 10693 (1E6), ATCC HB 10694 (HC-1B11), ATCC HB 10695 (7A6), and ATCC HB 10696 (8B8) or is monoclonal antibody TS2/9.
13. The method according to claim 12, wherein the monoclonal anti-LFA-3 antibody is produced by a hybridoma selected from the group of hybridomas having Accession Nos. ATCC HB 10695 (7A6) and ATCC HB 10693 (1E6).
14. The method according to claim 8, wherein the agent is a chimeric recombinant anti-LFA-3 antibody homolog.
15. The method according to claim 9, wherein the agent is a chimeric recombinant anti-CD2 antibody homolog.
16. The method according to claim 8, wherein the agent is a humanized recombinant anti-LFA-3 antibody homolog.
17. The method according to claim 9, wherein the agent is a humanized recombinant anti-CD2 antibody homolog.



18. The method according to claim 8, wherein the agent is selected from the group consisting of an Fab fragment, an Fab' fragment, an F(ab')<sub>2</sub> fragment, an F(v) fragment and an intact immunoglobulin heavy chain of an anti-LFA-3 antibody homolog.

19. The method according to claim 9, wherein the agent is selected from the group consisting of an Fab fragment, an Fab' fragment, an F(ab')<sub>2</sub> fragment, an F(v) fragment and an intact immunoglobulin heavy chain of an anti-CD2 antibody homolog.

20. The method according to claim 5, wherein the agent is a soluble LFA-3 polypeptide.

21. The method according to claim 4, wherein the agent is a soluble CD2 polypeptide.

22. The method according to claim 20, wherein the agent is a soluble LFA-3 polypeptide selected from the group of polypeptides consisting of AA<sub>1</sub>-AA<sub>92</sub> of SEQ ID NO:2, AA<sub>1</sub>-AA<sub>80</sub> of SEQ ID NO:2, AA<sub>50</sub>-AA<sub>65</sub> of SEQ ID NO:2, and AA<sub>20</sub>-AA<sub>80</sub> of SEQ ID NO:2.

23. The method according to claim 1, wherein the mammal is a human.

24. The method according to claim 1, wherein the agent is administered at a dose between about 0.001 and about 50 mg agent per kg body weight.

25. The method according to claim 24, wherein the agent is administered at a dose between about 0.01 and about 10 mg agent per kg body weight.

26. The method according to claim 24, wherein the agent is administered at a dose between about 0.1 and about 4 mg agent per kg body weight.

27. The method according to claim 24, wherein the dose is administered once to three times per week.

28. The method according to claim 24, wherein the dose is administered once to three times per day.

29. The method according to claim 28, wherein the dose is administered about one to three times daily for between 3 and 7 days.

30. The method according to claim 29, wherein the dose is administered about one to three times daily for between 3 and 7 days on a monthly basis.

31. The method according to claim 1, wherein the agent is administered intravenously, intramuscularly, subcutaneously, intra-articularly, intrathecally, periostally, intratumorally, intralesionally, perilesionally by infusion, orally, topically or by inhalation.

32. The method according to claim 31, wherein the agent is administered intramuscularly, intravenously or subcutaneously.

33. The method according to claim 4, wherein the agent is linked to one or more members independently selected from the group consisting of anti-LFA-3 antibody homologs, soluble CD2 polypeptides, cytotoxic agents and pharmaceutical agents.

34. The method according to claim 5, wherein the agent is linked to one or more members independently selected from the group consisting of anti-CD2 antibody homologs, soluble LFA-3 polypeptides, cytotoxic agents and pharmaceutical agents.

35. The method according to claim 34, wherein the agent is a polypeptide consisting of a soluble LFA-3 polypeptide linked to an immunoglobulin hinge and heavy chain constant region or portions thereof.

36. The method according to claim 35, wherein said polypeptide is LFA3TIP (SEQ ID NO:8).

37. The method according to claim 1, wherein the condition is UV damage.

38. A method of preventing or treating psoriasis comprising the step of administering to a mammal[, including a human,] a composition comprising an agent which binds to LFA-3 or CD2 selected from the group consisting of a CD2 polypeptide, an LFA-3 polypeptide, an anti-CD2 antibody homolog, and an anti-LFA-3 antibody homolog, in combination with a therapy selected from the group consisting of PUVA, chemotherapy and UV light.

39. The method of claim 38, wherein said agent is a CD2 polypeptide.

40. The method of claim 39, wherein said CD2 polypeptide is a soluble CD2 polypeptide.

41. The method of claim 38, wherein said agent is an LFA-3 polypeptide.

42. The method of claim 41, wherein said LFA-3 polypeptide is a soluble LFA-3 polypeptide.

43. The method of claim 42, wherein said soluble LFA-3 polypeptide is a soluble LFA-3 polypeptide fused to all or part of an immunoglobulin heavy chain region and all or part of a heavy chain constant region.

44. The method of claim 43, wherein said soluble LFA-3 polypeptide is LFA3TIP (SEQ ID NO:8).

45. The method of claim 38, wherein said agent is an anti-CD2 antibody homolog.

46. The method of claim 45, wherein said anti-CD2 antibody homolog is a humanized recombinant anti-CD2 antibody homolog or chimeric recombinant anti-CD2 antibody homolog.

47. The method of claim 38, wherein said agent is an anti-LFA-3 antibody homolog.

48. The method of claim 47, wherein said anti-LFA-3 antibody homolog is a humanized recombinant anti-LFA-3 antibody homolog or chimeric recombinant anti-LFA-3 antibody homolog.

49. The method according to claim 38, wherein the agent is a soluble LFA-3 polypeptide selected from the group consisting of AA<sub>1</sub>-AA<sub>92</sub> of SEQ ID NO:2, AA<sub>1</sub>-AA<sub>80</sub> of SEQ ID NO:2, AA<sub>50</sub>-AA<sub>65</sub> of SEQ ID NO:2, and AA<sub>20</sub>-AA<sub>80</sub> of SEQ ID NO:2.

50. The method according to claim 38, wherein the mammal is a human.

51. The method of claim 1, wherein the therapy is UV light therapy.

52. The method of claim 38, wherein the therapy is UV light therapy.

53. A method of preventing or treating psoriasis comprising the step of administering to a mammal a composition comprising a soluble LFA-3 polypeptide fused to all or part of an immunoglobulin heavy chain region and all or part of a heavy chain constant region in combination UV light therapy.

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54. The method of claim 53, wherein said soluble LFA-3 polypeptide is LFA3TIP  
(SEQ ID NO:8).